I. Preliminary Remarks

Attached hereto as Appendix A is a marked-up version of the changes made to the claims by the current amendment. Appendix A is captioned "**Version with markings to show changes made.**" Also, for the Examiner's convenience, attached hereto as Appendix B, is a complete list of the claims upon entry of the instant amendment. Appendix B is entitled "**Clean copy of claims pending in U.S. Serial No. 09/244,683 after entry of amendment filed September 20, 2002.**"

As an initial matter in reviewing the file history of the instant application, Applicants note that in paper 5, Examiner Draper had indicated that, but for the rejections under 35 U.S.C. §112, second paragraph and the obviousness-type double patenting rejections, claims 74-76 and 103-114 would be allowable if rewritten in an independent form. As such, Applicants believe that the subject matter of claims 74-76 and 103-114 is allowable even in the absence of the following response, and Applicants request further clarification for the record. Nonetheless, in the following response, Applicants address all of the rejections articulated by Examiner Bunner in paper 12.

II. Status of the Claims

Claims 71-114 are under consideration in the instant application. These claims stand variously rejected under 35 U.S.C. §112 first paragraph for lack of enablement and lack of written description, under obviousness-type double-patenting and 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the invention. Applicants respectfully traverse the rejection.

III. Objections to Specification and Claim 104.

Applicants thank the Examiner for holding the objection to the specification regarding the sequence compliance, priority, the Brief Description of the Drawings and references to other patent applications in abeyance until all other issues are resolved. Applicants renew the request and are in the process of preparing a separate paper that addresses these issues.

Claim 104 was objected to as being in an incorrect form for lacking a period at the

end of the claim. The amendment presented above places a period at the end of the claim thereby effecting the requested correction.

IV. Obviousness-type double-patenting

Applicants thank Examiner Bunner for holding the obviousness-type double patenting rejection in abeyance. Applicants renew their request to hold the double-patenting rejections in abeyance until such a time as the remaining issues have been addressed and allowable subject matter has been procured. At that point Applicants will furnish a terminal disclaimer, if necessary. The Examiner's discretion in this matter is solicited.

V. Rejections under 35 U.S.C. §112, first paragraph for lack of enablement are overcome and should be withdrawn

Claim 71-114 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not enabling a person skilled in the art to make and use the claimed invention commensurate in scope with these claims. Applicants respectfully traverse.

The Examiner states that the specification is enabling for a composition which comprises an effective amount of human stem cell factor (SCF) polypeptide and one or more cytokines in a pharmaceutically acceptable carrier wherein the SCF composition enhances hematopoiesis. However, the Examiner maintains that the specification "does not reasonably provide enablement for a composition which comprises a therapeutically effective amount of SCF or biologically active fragment or analog thereof and one or more cytokines in a pharmaceutically acceptable carrier wherein the composition is effective to treat hematopoeitic disorders, epithelial cell disorders, stromal cell disorders, neural disorders, pigmentation disorders, and germ cell disorders." (Office Action, paper 12, page 3). In addition, in contradiction to the statements made by Examiner Draper in paper 5, Examiner Bunner in paper 12 further asserted that the specification does not provide reasonable enablement for the SCF polypeptides consisting of the amino acid sequence set out as 1-100, 1-110, 1-120, 1-123, 1-127, 1-133, 1-141, 1-145, 1-148, 1-152, 1-156, 1-157, 1-158, 1-159, 1-160, 1-161, 1-163, 1-166, 1-168, 1-173, 1-178, 1-180, 1-183, 1-185, 1-188 and 1-189 as set out in Figuures 42A-C and 44A-C (*i.e.*, part of the subject matter of claims 75 to 76, previously indicated as allowable by

Examiner Draper). Applicants respectfully traverse the rejections and request reconsideration.

The claims of the present invention generally are directed to:

> "A composition which comprises a therapeutically effective amount of stem cell factor (SCF) polypeptide or biologically active fragment or analog thereof and one or more cytokines in a pharmaceutically acceptable carrier." (Claim 71).

Additional claims recite specific amino acid sequences for the stem cell factor (claims 74, 75, 76) and further recite that the SCF is effective to treat epithelial cell disorders (claims 81, 82), stromal cell disorders (claims 83, 84) neural disorders (claims 85, 86), pigmentation disorders (87, 88) and germ cell disorders (claims 89, 90). Other claims recite cytokines in the pharmaceutically acceptable carrier (claims 91 to 102) and the delivery formulations of the pharmaceutically acceptable carrier (*e.g.*, controlled release, parenteral, pulmonary, nasal, or topical delivery claims 103 to 114). Applicants submit that each of these claims is fully enabled by the specification as filed and provide the following discussion for the Examiner's consideration.

The specification as filed teaches that SCF has a "central role in embryogenesis and hematopoiesis" and demonstrates its "capacity for treatment of various stem cell deficiencies." (specification page 18, lines 20-24). The full length human stem cell factor is SCF 1-248 amino acids in length. The Examiner agrees that the specification is "enabling for the SCF polypeptide consisting of amino acid sequences 1-162, 1-164, 1-165 of SEQ ID N:46; 1-130, 1-137, 1-248, 2-164, 5-164, 11-164 of SEQ ID NO:61 and 1-220 of SEQ ID NO:63" (See Office Action, paper 12, page 3). These specific polypeptides are fragments of full-length SCF.

The specification expressly teaches how to monitor the *in vitro* activity of a given SCF polypeptide. For example, in Example 1, between pages 31 and 34, the specification provides a teaching of how to determine the effect of a given SCF on early hematopoietic cells (using a high proliferation potential colony forming cell (HPP-CFC) assay); how to determine whether a given SCF will cause proliferation of an IL-4 dependent murine cell line (using a MC/9 assay); and how to evaluate the effect of a given SCF on normal undepleted bone marrow

(using a CFU-GM assay). Each of these assays were well known to those of skill in the art when the application was filed (see for example, Zsebo *et al.*, *Blood*, 71 962-968, 1988; Broxmeyer *et al.*, *Exp. Hematol.*, 5, 87 1977 both referenced in the specification), and it was a matter of routine experimentation to set up one or more of these assays to elucidate the effect of a given factor.

The specification also provides specific teachings of how to monitor the effects of a SCF composition *in vivo*. At page 104 of the specification, Applicants have taught that SCF corrects macrocytic anemia and other phenotypic disorders of a bone marrow transplant mouse model. Additional methods for monitoring *in vivo* efficacy of SCF compositions are demonstrated in tests performed in primates, shown at page 108 of the specification. These latter tests are performed using the $hSCF^{164}$ and $hSCF^{165}$ (*i.e.*, fragments of SCF). In addition to these assays, Example 28 expressly teaches how to make numerous SCF analogs and fragments (see specification at pages 182-85). Example 28 goes on to expressly list the numerous analogs and fragments that have been made (*e.g.*, specification page 182-185, which are discussed in further detail in Applicants response to the rejection under 35 U.S.C. §112, first paragraph for lack of written description in Section VI below. The remarks in that section are incorporated into the present section by reference).

Clearly, the above teachings provide specific and substantial guidance to those of skill in the art of how to set up, perform and evaluate assays designed to determine whether a given SCF (be it full length or a fragment) has a desired activity. Applicants disagree with the Examiner that it would require undue experimentation to determine whether a SCF polypeptide consisting of the amino acid sequence set out as 1-100, 1-110, 1-120, 1-123, 1-127, 1-133, 1-141, 1-145, 1-148, 1-152, 1-156, 1-157, 1-158, 1-595, 1-160, 1-161, 1-163, 1-166, 1-168, 1-173, 1-178, 1-180, 1-183, 1-185, 1-188, 1-189 as set out in Figures 42A-C and 44A-C have specific activity. Applicants specifically described that these fragments and analogs of SCF have been produced (see page 182-185 of the specification). Moreover, at pages 116-127, the specification expressly details methods for purifying recombinant SCF products. This disclosure combined with the disclosure of the sequences of the full length SCF and the express teachings of how to make other fragments, analogs and derivatives from the SCF sequences exemplified by the Applicants in Example 28, fulfill the statutory requirements of teaching how to make the claimed compositions. It would be a matter of mere routine experimentation to run these and any other

fragments, and analogs of SCF through any of the battery of assays exemplified by the Applicants in the specification, or indeed any of the other assays known to those of skill in the art at the time the application was filed, to determine the specific activity of such fragments, and analogs.

Applicants take issue with the Examiner's assertion that a "large quantity of experimentation would be required . . . to determine any structural or functional characteristics of the SCF fragments comprising amino acids . . . identified by the Examiner to be non-enabled". (Office Action, paper 12, page 5). This is not the correct standard by which to determine whether claims to a given composition are enabled. Enablement is not precluded by the necessity for some experimentation, indeed it is inevitable that there may be some quantity of experimentation required. The mere fact that some degree of experimentation may be required is not the determinative factor in the scope of enablement; it is only when the level of experimentation becomes undue that it is fatal to the enablement of an invention. Thus, the key word is ***undue***, not experimentation. *In re Wands* 858, F.2d 731, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). A determination of what constitutes undue experimentation in a case requires application of a test of reasonableness giving regard to the nature of the invention and the state of the art. *Id.* The test is not merely quantitative since a considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance. *Id.* Applying the standard articulated in *In re Wands*, the present specification provides not only a reasonable but a copious amount of guidance to one of skill in the art to who wants to determine the SCF specific activity of an analog, fragment or derivative. Thus, the invention is objectively enabled and nothing more is required to satisfy the first paragraph of §112. *In re Marzocchi*, 169 USPQ 367,369 (CCPA 1971).

Furthermore, it is a well known tenet of the law that a specification disclosure need not teach, and ***preferably should omit***, what is well known to those of skill in the art. *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). As long as the specification contains at least one method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claimed invention, then the enablement requirement under 35 U.S.C. §112 is satisfied. *In re Fisher*, 166 USPQ 18, 24 (CCPA, 1970); MPEP 2164.01(b). Given the level of skill in the art, the skilled artisan could take any of the fragments, analogs or derivatives

expressly taught in the specification (*e.g.*, pages 182-185) and perform one or more assays such as, *e.g.*, the *in vivo* and *in vitro* assays described in the specification or related assays known in the art at the time the application was filed and determine the specific activity of the fragments. This is routine experimentation. Indeed, one of skill in the art could make additional derivatives of the SCF sequences expressly disclosed in the specification using the teachings of the specification (see *e.g.*, Example 28) or standard techniques well known to those of skill in the art and still perform the same assays without undue experimentation. This is because the enablement requirements of the statute are satisfied when the specification disclosure, ***taken with the teachings in the art***, teaches an effective process for making the claimed compositions from known starting materials, and the specification describes methods of using the claimed compositions. *Ex parte Gastambide, Thal, Rohrbacj and Laroche* , 189 USPQ 643, 645 (PTO Bd. App. 1974).

The Examiner also is inaccurate in stating that "the structure and function of every SCF fragment and analog claimed is not disclosed in such a manner that one skilled in the art could make and use them without undue experimentation." (Office Action, paper 12, page 5). Again this is not a correct statement of what is required from a specification disclosure to meet the legal requirements of enablement. In asking for such a disclosure, the Examiner's request is tantamount to requesting working examples of all the fragments and analogs. Such an onerous requirement is in direct opposition to the established tenet that working examples are not required for an enabling disclosure. *In re Robins*, 166 USPQ 552 (CCPA 1970); *In re Borkowski*, 164 USPQ 642, 645 (CCPA 1970). The first paragraph of §112 requires nothing more than objective enablement. *In re Marzocchi*, 169 USPQ 367 (CCPA 1971). Thus, an example may be a "working" or a "prophetic" example, indeed the specification need not contain an example at all if the invention is otherwise disclosed in such a manner that one of skill in the art will be able to practice it without undue experimentation. Again, the present specification provides a disclosure of how to make analogs and fragments of SCF; it teaches numerous specific analogs and fragments; it also provides guidance on how one of skill in the art may produce additional biologically active variants, fragments, derivatives, homologs or analogs thereof. Further, the specification details how to determine the biological activity of such polypeptides. It is well within the skill of artisans practiced in this field to conduct and compare the described assays as a matter of routine laboratory practice.

Applicants also wish to address the Examiner's contention that the "present invention is unpredictable and complex" because "one skilled in the art may not necessarily be able to generate the infinite number of SCF derivatives recited in the claims and screen the same for activity." (Office Action, paper 12, page 7). Applicants disagree with the Examiner that the skilled person would not be able to predict that variants and analogs of the instant application would have the same functional activities as the human SCF fragments. Again, Applicants point out that the specification has taught, at some length, the activity of both human and rat SCF. The Examiner agrees that for at least 10 fragments, the specification also has provided express enablement in the form of specific working examples. Applicants have shown that other fragments can and have been generated and have taught how to make yet further analogs and fragments. The Examiner has cited no factual evidence or scientific reasoning that would support the contention that undue experimentation would be required to determine whether or not the variants or analogs have the same functional activities as the human SCF fragments specifically exemplified in the specification. Given the teachings of the specification, no "prediction" or prophesy is necessary. The skilled artisan merely sets up the assays as described in the specification and obtains the functional read-out. Given that the specification has taught how to do this for not only the full length rat and human SCF sequences, but also for at least 10 fragments of the SCF, there is no factual or scientific reason for why additional fragments could not be assayed in the same fashion to yield the same or similar results. Such ***qualitative*** factual or scientific evidence, and ***not*** the mere fact that additional ***quantitative*** experimentation may be needed, must underlie the rejection of the pending claims and in the absence of the same, a *prima facie* case of lack of enablement has not been established for any of the rejected claims.

Given the detailed teachings of the specification and the level of skill in the art, it is well within the skill of artisans practiced in this field to prepare the compositions of the present invention as a matter of routine practice. In view of the foregoing, Applicants respectfully submit that the specification and claims are in full compliance with enablement requirement of 35 U.S.C. §112, first paragraph. Therefore, Applicants request that the rejections be withdrawn and the claims be reconsidered for allowance.

VI. Rejections under 35 U.S.C. §112, first paragraph for lack of written description are inapplicable and should be withdrawn.

Claims 71-114 were rejected under 35 U.S.C. §112 first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of claimed the invention at the time the application was filed. Applicants respectfully traverse.

The Examiner asserts that the "specification does not teach all analogs or variant of the SCF polypeptide of the instant invention" and goes on to state that the "description of ten specific SCF polypeptide fragments that enhance hematopoiesis not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all biologically active fragments and analogs of SCF." (Office Action, paper 12, page 9). The Examiner posits that with the exception of the SCF polypeptides consisting of the amino acid sequences of 1-162, 1-164, 1-165 of SEQ ID N:46; 1-130, 1-137, 1-248, 2-164, 5-164, 11-164 of SEQ ID NO:61 and 1-220 of SEQ ID NO:63, "the skilled artisan cannot envision the detailed structure and function of all possible fragments and analogs encompassed by the claims, and therefore conception is not achieved until reduction to practice has occurred" (Office Action, paper 12, page 10).

In the first instance, the Examiner is incorrect that only 10 specific SCF polypeptide fragments are expressly described in the specification. Notwithstanding the Examiner's position of lack of enablement of such compositions (an argument that is refuted in section VI above and is incorporated into the present section V by reference), it is beyond question that there is an adequate written description in the specification for numerous other fragments that were made and in the possession of the Applicants before the application was filed. For example, the Examiner is referred to the specification, which explicitly states that:

> "After fermentation and harvesting of cells, many folded, oxidized purified SCF analogs have been recovered by the methods outlined in Example 10. These include (by the numbering of Figure 42) SCF^{1-189}, SCF^{1-188}, SCF^{1-185}, SCF^{1-180}, SCF^{1-156}, SCF^{1-141}, SCF^{1-137}, SCF^{1-130}, SCF^{2-164}, SCF^{5-164}, SCF^{11-164}, and (by the numbering of

Figure 44) SCF^{1-161}, SCF^{1-160}, SCF^{1-152}, SCF^{1-152}. Like SCF^{1-164}, and SCF^{1-165} (Examples 17 and 27), these analogs are all dimeric." Specification page 185, lines 5-15.

This section of the specification also provides exemplary specific activities for these SCF fragments. Additionally, the specification at page 182, lines 6-28 provides that:

> "Site-directed mutagenesis has been used to prepare plasmids with initiating methionine codon followed by codons for amino acid 1 to 178, 173, 168, 166, 162, 161, 160, 159, 158, 157, 156, 148, 145, 141, and 137 using the numbering of Figure 15C. . . . The oligonucleotides for each cloning were designed to substitute a stop codon for an amino acid codon at the appropriate position for each analog."

This section of the specification further provides a detailed experimental protocol to teach an exemplary method of how to produce such analogs. The Examiner also is referred to the next paragraph on the same page, which states that:

> "Plasmids with initiating methionine codon followed by codons for amino acids 1 to 130, 120, 110, 100, 133, 127 and 123 (using the number of Figure 42) have been made using the polymerase chain reaction." Specification page 182, lines 29-33.

In addition, Applicants have explicitly taught that:

> "Plasmids with initiating methionine codon followed by codons for amino acids 1 to 164, 5 to 164 and 11 to 164, (using the number of Figure 42) were also made using the polymerase chain reaction." Specification page 183, lines 6-9.

The specification at pages 182 through 185 provides additional details of specific analogs. The Examiner also is referred to claims 30, 49, and 70 as originally filed which further

provide additional written description support for analogs and derivatives. Given these explicit recitations of analog compositions of the claimed invention, Applicants submit that the Examiner's position that only 10 fragments are supported by the written description of the specification is incorrect as a matter of fact.

Furthermore, Applicants note that the rejection as articulated discusses whether or not one can "predict the functional activities of every SCF fragment or analog recited in the claims." The issue of predictability is one which falls within the purview of the enablement requirement of 35 U.S.C. §112, and not the written description requirement of that section of the statute. These two requirements of 35 U.S.C. § 112, first paragraph, are "separate and distinct" from each other. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). Applicants have already discussed that the claimed subject matter is objectively enabled by the specification as filed.

The essential goal of the written description requirement is to clearly convey the information that an Applicant has invented the subject matter which is claimed. This goal is to clearly convey to those skilled in the art that the Applicant had possession of the claimed invention as of the date of invention. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 U.S.P.Q.2d 1398, 1405 (Fed. Cir. 1997). Applicants have met this burden of showing possession of many more analogs than the 10 recited by the Examiner. In light of these numerous recitations in the specification and the listing of these sequences therein, it is wholly reasonable that one of skill in the art could and would envision the detailed structure and function of the SCF polypeptide fragments and analogs encompassed by the claims. A person reading the specification in its entirety would understand that the instant inventors invented and exemplified such SCF polypeptide fragments and analogs. Hence, the written description requirement, separated and apart from the enablement requirement, also is satisfied for the entire scope of the claimed invention.

In light of the explicit teachings of the present invention, Applicants submit that the rejection of the claims based on 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn.

VII. Rejections under 35 U.S.C. §112, second paragraph are overcome by the amendments and should be withdrawn.

The Examiner maintained-in-part the rejection of claims 71-114 under 35 U.S.C. §112, second paragraph. More particularly, the Examiner rejected claims 91-102 for using the acronyms IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, EPO, G-CSF, GM-CSF, CSF-1, IGF-1 and LIF." While Applicants maintain that these acronyms are well known to those of skill in the art to render the claims sufficiently clear, in an effort to expedite the prosecution of this case to allowance, Applicants have replaced the abbreviations with the full names of the associated cytokines. These amendments do not add new matter. Briefly, throughout these claims the abbreviation "IL" has been replace with the term "interleukin," the abbreviation "EPO" has been replaced with the term "erythropoietin," the term "G-CSF" has been replaced with "Granulocyte Colony-stimulating Growth Factor", the abbreviation "GM-CSF" has been replaced with the term "Granulocyte-Macrophage Colony-Stimulating Factor," the abbreviation "CSF-1" has been replaced with the term "Colony Stimulating Factor-1," the abbreviation "IGF-1" has been replaced with the term "Insulin-like Growth Factor-1," and the abbreviation "LIF" has been replaced with the term "Leukemic Inhibitory Factor."

In view of the foregoing response, Applicants submit that the outstanding rejection of the claims under 35 U.S.C. §112, second paragraph is overcome. Applicants request that the rejection be withdrawn and the claims be reconsidered for allowance.

VIII. Conclusion.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

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Appendix A

Version With Markings to Show Changes Made

91. [Once Amended] The composition of claim 79, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

92. [Once Amended] The composition of claim 80, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

93. [Once Amended] The composition of claim 81, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

94. [Once Amended] The composition of claim 82, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor,

~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

95. [Once Amended] The composition of claim 83, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

96. [Once Amended] The composition of claim 84, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

97. [Once Amended] The composition of claim 85, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

98. [Once Amended] The composition of claim 86, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor,

~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

99. [Once Amended] The composition of claim 87, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

100. [Once Amended] The composition of claim 88, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

101. [Once Amended] The composition of claim 89, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor, ~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

102. [Once Amended] The composition of claim 90, wherein the composition contains at least one cytokine selected from the group consisting of ~~IL-1~~ Interleukin-1, ~~IL-2~~ Interleukin-2, ~~IL-3~~ Interleukin-3, ~~IL-4~~ Interleukin-4, ~~IL-5~~ Interleukin-5, ~~IL-6~~ Interleukin-6, ~~IL-7~~ Interleukin-7, ~~IL-8~~ Interleukin-8, ~~IL-9~~ Interleukin-9, ~~IL-10~~ Interleukin-10, ~~IL-11~~ Interleukin-11, ~~IL-12~~ Interleukin-12, ~~EPO~~ erythropoietin, ~~G-CSF~~ Granulocyte Colony-stimulating Growth Factor, ~~GM-CSF~~ Granulocyte-Macrophage Colony-Stimulating Factor,

~~CSF-1~~ Colony Stimulating Factor-1, ~~IGF-1~~ Insulin-like Growth Factor-1, and ~~LIF~~ Leukemic Inhibitory Factor.

104. [Once Amended] The composition of claim 77, wherein the composition contains a pharmaceutically effective carrier for the controlled release of SCF and other cytokines in the composition.